Thank you. Good morning.

It's been a long but I hope informative & productive week for you.

Your presence here this morning suggests that you're not among those who eat dessert first.

By that, I mean to say that we have saved the best part of DARPA's S&T menu - biology - almost for last.

You know, biology isn't what it used to be when I was in high school - frogs, scalpels, iodine stains, phylogeny, evolution, Mendelian genetics, and anatomy.

Fascinating stuff to be sure.

No artificial system I know of yet matches the beauty, complexity and functionality of living organisms.

But the very complexity of biological systems challenges our ability to understand them in fundamental terms. Physicists have been pushing hard for the past 100 or so years to describe the fundamental laws governing the behavior of matter, light and electricity; and it is now imaginable that they will achieve the ultimate goal - a final theory of everything.

Chemistry and materials science began maturing in the first half of the 20th century and combined with physics have contributed to revolutionary technologies that have forever changed the way we live.

In comparison, biology has lagged behind physics and chemistry.

But you need to understand that biology didn't get its "periodic table of the elements" until less than 50 years ago.

In 1951, a young and brash American biologist began to work with a British physicist to determine the structure of DNA.

Just a few years earlier, DNA -- deoxyribonucleic acid -- had been identified as the chemical of which genes were made.

Genes - those mysterious determinants of heredity - were a concept first elaborated by Mendel in 1865 to explain how pea plants inherit traits such as color or size; this was just 8 years before Maxwell published his treatise on electricity and magnetism.

What might a gene actually be?

Well, it took another hundred years until we realized that genes were composed of DNA.

And then, a momentous event occurred in 1953.

That year, Watson and Crick's brilliant interpretation of an X-ray diffraction pattern led them to realize that the structure of DNA - the famous double helix - provided a stunningly simple molecular explanation for how genes are replicated.

Or, as they purposefully understated it in their Nature paper: "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material".

Their famous structure also provided the molecular explanation for how genes control the properties of organisms.

Their discovery of the structure of DNA profoundly changed biology.

For it launched a scientific revolution that has matured to the point where it has become imaginable that we will be able to mimic and control biological systems based on a fundamental understanding of their molecular parts. Now, although the structure of DNA was solved almost 50 years ago, technologies for cloning and sequencing DNA were developed only about 25 years ago; and the ability to rapidly determine the entire sequence of an organism has been around for only five years.

But what an impact the genomics revolution is already having on biology!

For the DNA sequence of an organism - when interpreted and coupled to other pieces of information about the organism - provides a strategy for determining the molecular anatomy of that organism.

Because the DNA sequence provides a way to begin exploring an organism's molecular composition, last year DARPA decided to make sure that the Slide 5 complete DNA sequences of potential biological warfare agents would be determined.

The sequence of a pathogen's genome is, in a sense, it's blueprint, it's plan for making you sick.

The DARPA genomic sequencing effort will, therefore, enable us to examine that blueprint and learn fundamentally important information about the identity and function of a pathogen's molecular anatomy.

The sequence information we obtain from pathogens will enable us to design rational strategies for developing diagnostic approaches for detecting biowarfare agents in the environment and in clinical samples.

That information can also be used as a guide for developing therapeutic approaches for treating the consequences of infection by a biowarfare agent.

But I don't mean to overstate the significance of DNA sequence information.

For although a sequence will provide much new and valuable information about an organism, it's far from a complete description.

Try this analogy. Suppose I disassembled an F18 and made a list of its parts. I'll use trivial names for parts whose function I know - wheels, bolts, lights, seats - and serial numbers for parts whose functions I know nothing about.

Now suppose I show you my parts list.

Would you consider that list to be an adequate representation of a fighter plane?

The challenge in biology is to not only determine the identity of an organism's molecular parts - a simple cell, for example, might contain as many as 5000 different proteins - but to learn: What those parts do; What the structure of a part is; How the structure of a part determines its function; How the synthesis of a part is regulated; What other parts they interact with; And, most daunting of all, how all of the parts are integrated to function as a dynamic living system.

To decipher biological complexity will require the development and use of new physical and computational tools.

Thus, we will need to invent new devices capable of interrogating living cells and single molecules to help biologists characterize the physical properties of a cell's molecular components, determine their numbers and their location.

We will also require new mathematical approaches for analyzing massive quantities of information and reducing the dimensionality of primary data.

And we will require new computational tools to model and simulate the dynamic behavior of biological systems while remaining faithful to the physical and chemical behavior of system components.

So where does DARPA come into this picture? What is our role and what do we hope to gain from it? DARPA wishes to promote the development and use of modern tools from the physical and information sciences to generate fundamentally new information about complex biological systems.

We're interested in doing this because we would like to develop new capabilities for DOD based on a principled understanding of biological mechanisms.

By pursuing research at the intersection of biology with the physical and information sciences - that is with the technology communities that DARPA helped to create - we will overcome current limitations to understanding biological systems.

Such research will have an impact far beyond the new knowledge we generate about biological systems.

We believe that our research program at the intersection of biology with the physical and information sciences will lead to the development of fundamentally new ways to design and manufacture materials and devices; The knowledge we generate will inspire new ways for us to design, control and interact with artificial systems; It will provide new ways to think about how we capture, store and process information and new ways to create fault-tolerant software; It will provide new ways to monitor humans and living systems; And it will enable better defensive strategies against WMD via sensors, therapeutics, and protection.

There are many recent technology developments in the physical and information sciences to encourage our belief in the power of this interdisciplinary approach.

For example, CMOS-based microsystems technology - state-of-the-art fabrication facilities - can now, almost routinely, manufacture devices with length scales in the nanometer to micrometer range.

These are the very sizes required to interrogate single cells and characterize individual molecules from or within cells.

And in the information sciences increasingly powerful computational tools being developed for defense purposes - e.g. automatic target recognition - could be exploited and customized to assist in the analysis and interpretation of the data stream that will emerge from the interrogation of biological systems with CMOS-based technologies.

The first phase of DARPA's new emphasis on research at the interface of physical, information and biological systems is now underway.

This past year three DARPA offices - DSO, ITO and MTO - jointly issued a call for interdisciplinary grant proposals from universities. Program managers from all three offices co-managed the review process.

We received many outstanding ideas.

There were many outstanding ideas.

In the end we selected 6 proposals for awards that began this past summer.

The awards were made in two broad areas of basic research: neuroprocessing and biological regulatory networks.

But, the DARPA emphasis is not the research areas per se, relevant to DoD, tho they are in their own right.

The DARPA emphasis is rather in using these areas of research as fertile ground for developing productive interactions among the biological, informational, and physical sciences that will lead to the creation of innovative technologies.

Let me briefly describe each of those areas for you. Neuroprocessing.

How do our brains actually work?

The human brain is more than 3 times larger than a chimp brain.

Unless you were recently educated in Kansas, you probably recall that chimps are our nearest relatives.

Most of the difference in size between a chimp brain and a human brain can be accounted for by the development of a region of the brain called the neocortex.

If we had the ability to intercept and interpret signals from individual neurons and from large ensembles of neurons in the neocortex we would be listening to the "language" used by the neocortex as it processes information, controls behavior, and learns.

That is just the kind of information one needs to develop neuroprosthetic devices, for example, the kind that Clint Eastwood found to be so useful in Foxfire, one that works simply by thinking about it.

That kind of information might also provide us with a biologically inspired synthetic language for designing new computational algorithms for solving difficult signal processing or target recognition problems.

The awards we made to Arizona State University, Brown University, and Caltech will permit investigators there to develop new devices based on MEMS, carbon nanotubes, and other advanced microelectronic and optoelectronic technologies to interrogate and manipulate living brains and brain slices.

To complement the new devices, new computational methods must be developed to analyze and interpret the new information.

The computational methods being developed in our new neuroprocessing program include approaches that will use neural decoding algorithms for neural spikes and for local field potentials. In addition, the investigators will develop new methods for representing spatial components in distributed systems and use decision theoretic approaches for decoding brain signals.

Many technical hurdles will need to be overcome during the course of these investigations.

For example, the group at Arizona State will be focusing some of their effort on developing nanodevices made of materials that can be tolerated for long periods of time in a living brain. If they accomplish that task it would become possible to monitor neocortical signals for long periods of time in an animal as it moves, learns and responds to stimuli.

The common focus in these efforts is the interaction between a biological information processor - the brain - and synthetic networks of nano and micro- devices. By focusing on those interactions we hope to develop a deeper understanding of the neural and synaptic organization of the brain and to eventually use that understanding as a guide to designing new DOD capabilities in signal processing, computation, and the human-machine interface.

The second broad area we have invested in is in a newly developing field we call biological regulatory networks.

I introduced you to the concept earlier when I discussed both the power and limitation of learning the genomic sequence of an organism and the inadequacy of a parts list to fully describe a living system.

If we hope to deeply understand and to manipulate living systems we will have to develop tools and representations that capture the complex behavior of their individual cells.

And to do that we will need to develop ways to observe the behavior and components of single cell.

So, the focus of the biological regulatory network thrust is the single cell.

Investigators at Princeton, MIT and Stanford will begin to use technologies developed by their physical and information science colleagues to begin interrogating and analyzing single cells from experimentally tractable biological systems - bacteria, yeast, worms, mammalian cells grown under defined conditions in culture.

The technologies that will be developed and used include devices that can manipulate single DNA molecules for physically mapping the complete set of proteins that control gene expression in a cell; High-speed 2-photon microscopy for localizing molecules inside of cells; Micro-injection and microtemplate arrays for manipulating hundreds and thousands of individual cells at a time; And high-throughput microanalytical devices for fractionating, sorting and manipulating cells and their components. Information technology tools for this research area include the development of new algorithms applied to data collection to detect patterns and networks; They include models for the operation of biomolecular networks governing growth and death; And they include the development of software based on hybrid control theory for distributed, asynchronous control architectures.

Our investment in this research area should provide us with a systems level view of how cells behave.

The systems level perspective will enable many new capabilities for the warfighter including better ways to circumvent the toxic or even lethal effects of exposure to chemical and biological warfare agents and the design of systems that will use biological components to compute.

DARPA's Defense Sciences Office is investing in several other areas involving biology - Tissue Based Biosensors, Controlled Biological Systems, and metabolic engineering - that will provide other kinds of capabilities for the warfighter.

I'd like to begin wrapping up this talk by briefly describing two of these programs for you - Tissue Based Biosensors and metabolic engineering.

Tissue Based Biosensors is based on a very simple idea. What if we could use cells and tissues directly to detect dangerous chemicals in environmental or even clinical samples? Coal miners used to rely on canaries as an early warning system for the presence of dangerous levels of gas.

Suppose cells could be engineered to respond to the presence of dangerous chemicals.

If they could and if they could be made rugged, it is imaginable that they could be used directly in a canary-like fashion.

Such a capability would solve a major problem that could develop in the future.

We're getting pretty good at detecting the nasty chemical and biological agents we know about. One can use antibodies or DNA probes for example to detect small quantities of an agent with high degree of specificity and reliability.

But what if the agent is something we have never seen before?

The warfighter doesn't necessarily care about the identity of an agent.

He simply wants to know if it is hazardous.

Hence, a detection system based on the responses of biological material to samples could provide the answer.

Thus the concept behind the tissue based biosensors program is to develop technologies that use living cells and tissues in devices that report the physiological consequences of exposure to environmental samples.

Such devices will be capable of broadly classifying the sample: Is it hazardous? Is it a chemical or biological agent? What is its mechanism of action? What might be the long-term consequences of exposure?

There are many technical barriers to be overcome in the development of a tissue-based biosensor - sample collection and preparation; The design and engineering of a system that would operate with cells; Engineering the detection capabilities to be sensitive, specific, rapid, and proportional to dose; And developing data acquisition and analysis tools on which to base decisions about the presence or absence of a threat.

These are all hard problems that will be addressed over the next few years by our Tissue based biosensors program and its program manager, Alan Rudolph.

The other and last area of biological research I want to tell you about is a new effort at DARPA and is, somewhat, connected to the tissue based biosensor idea.

Our new program in metabolic engineering is going to attempt to develop technologies that would permit the long-term storage of cells and tissues.

The ability to provide fresh blood and blood products on the battlefield to a badly wounded warfighter depends on a logistics capability that is often hard to maintain.

What if medical supplies - such as blood - could be stored at room temperature in a dormant state and became usable on demand just by, say, adding water?

How might one engineer stability into cells?

Well, nature does this all the time!

Brine shrimp, algae, bacteria, and hibernating animals have, among them, a broad repertoire of mechanisms for slowing down, even shutting down, their metabolism to stabilize their cells against desiccation, cold, and even oxygen deprivation.

What if we could either engineer those traits into human cells - or at least learn how to elicit some of those capabilities that may well be lying latent in human cells - so as to enhance the storability and survivability of blood products?

We've begun to invest in some clever investigators who have ideas about how to go about developing the knowledge we will need to launch such a radically new technology for the warfighter.

Stay tuned!

By the way, DARPA is continuing efforts begun four years ago to develop counter measures against potential BW agents and to develop advanced diagnostics for the earliest possible detection of infection by such agents.

The unconventional pathogen counter measures and advanced diagnostics programs are now led by Drs. John Carney and Alan Rudolph, respectively.

I encourage you to contact them if you want more information about those programs.

In conclusion, I'd like to invite your help. You have the creative ideas. You do the hard work. You, and the organizations you represent, accomplish revolutionary advances on behalf of the warfighter. If biology is to provide the warfighter with new capabilities based on the use, manipulation, or mimicking of biological systems, we need to get you and your organizations involved.

If you have ideas and technologies that could be used to help us better understand and exploit biological systems in ways that are relevant to DOD, we want to hear from you. If you have ideas and technologies for creating biomimetic systems that could enhance DOD capabilities, we want to hear from you. And if you have ideas and platforms for using biological systems or bioinspired systems for enhancing a DOD capability, we want to hear from you. And finally, should you have any questions or comments about the programs I described please do not hesitate to contact me.

Thank you.